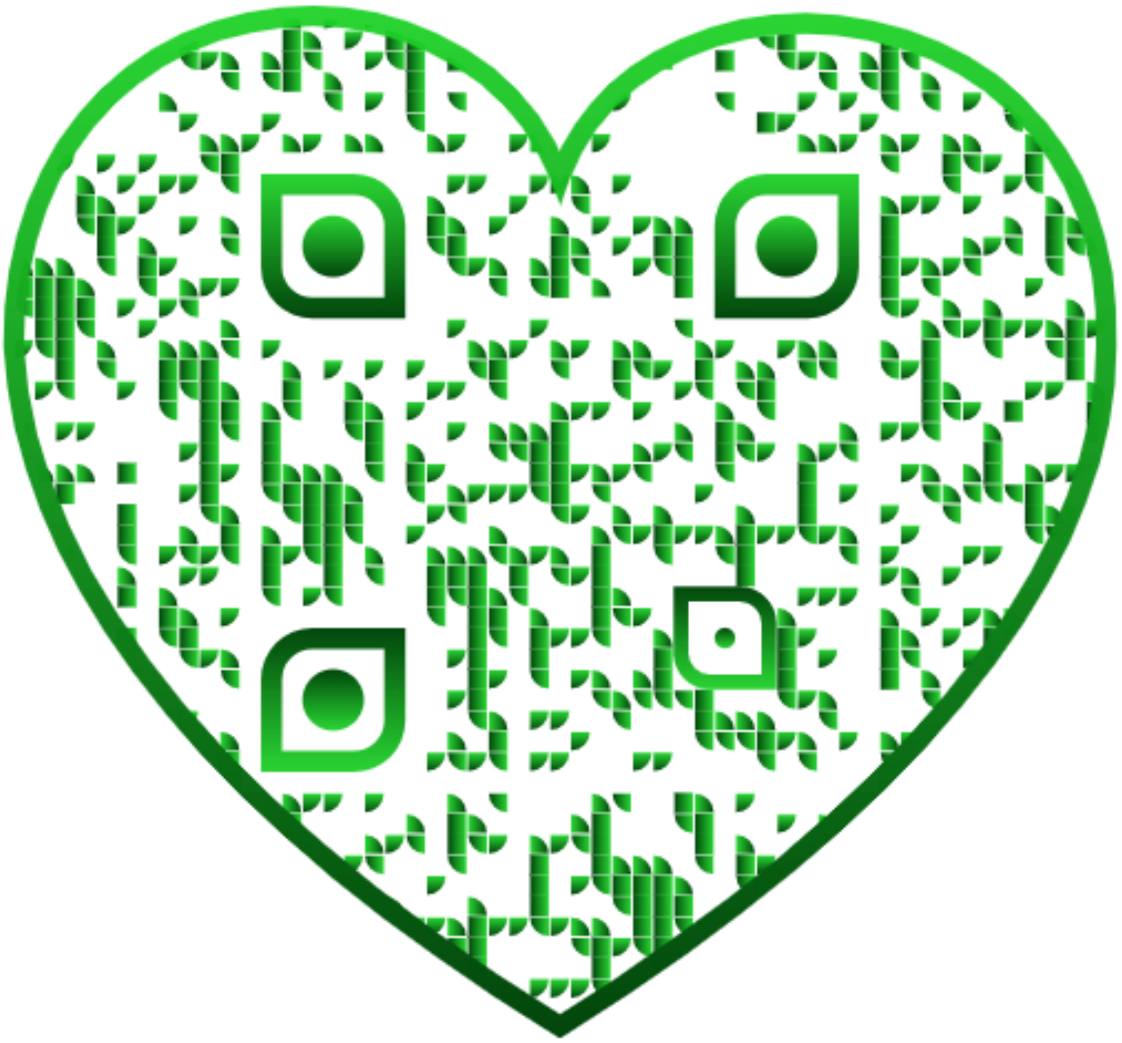
7. Rheology



Introduction

- Rheology
  - To describe the flow of liquids and the deformation of solids,
  - It is used to study and characterize paints, inks, doughs, road-building materials, cosmetics, dairy products, and other materials,
  - In pharmacy: formulation and analysis of products such as emulsions, pastes, suppositories, and tablet coatings …
    - These products acceptable consistency and smoothness and reproducibility?

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- Rheological characterization a material/product is very important, involved in:
  - Mixing and flow of materials,
  - Packaging into containers,
  - Removal prior to use,
    - Pouring from a bottle,
    - Extrusion from a tube,
    - Passage through a syringe needle

- The rheology of a particular product, also:
  - Can affect its patient acceptability,
  - Physical stability,
  - Biologic availability
  - Can influence the selection of processing equipment used in its manufacture

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- Based on the types of flow and deformation, materials can be placed in one of two categories:
  - Newtonian systems or
  - Non-Newtonian systems

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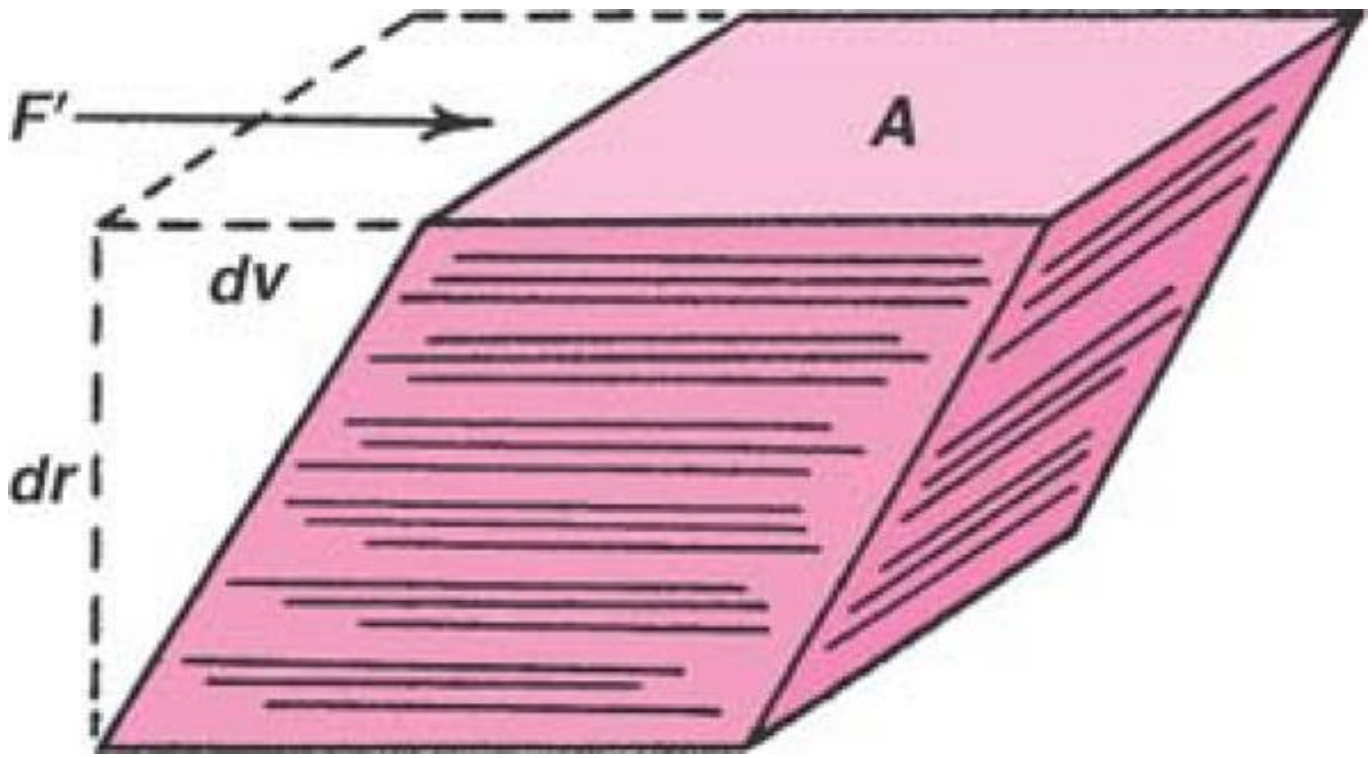
Newtonian Systems

Newton's Law of Flow

- Consider a "block" of liquid (similar to a deck of cards),
  - Where, the bottom layer is fixed in place and the top plane of liquid is moved at a constant velocity,
  - Each lower layer will move with a velocity directly proportional to its distance from the stationary bottom layer.


F'
A
dv
dr

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- The difference of velocity, dv, between two planes of liquid separated by an infinitesimal distance (dr) is the velocity gradient or **rate of shear** (dv/dr)
- The force per unit area, F'/A, required to bring about flow is called the **shearing stress** (F)
- Newton's law of flow:
  - "the higher the viscosity of a liquid, the greater is the force per unit area (shearing stress) required to produce a certain rate of shear (G)"

$$\frac{F'}{A} = \eta \frac{dV}{dr} \qquad \textbf{or} \qquad \eta = \frac{F}{G}$$

where η is the coefficient of viscosity (viscosity)

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- Viscosity
  - An expression of the resistance of a fluid to flow,
  - The higher the viscosity, the greater is the resistance,
  - The unit of viscosity is the poise, cgs units for poise are dyne sec cm^{-2} [(i.e., dyne sec/cm^2) or g cm^{-1} sec^{-1} (i.e., g/cm sec)]

$$\eta = \frac{F' dr}{A\, dv} = \frac{\text{dynes} \times \text{cm}}{\text{cm}^2 \times \text{cm/sec}} = \frac{\text{dyne sec}}{\text{cm}^2}$$

$$\frac{\text{dyne sec}}{\text{cm}^2} = \frac{\text{g} \times \text{cm/sec}^2 \times \text{sec}}{\text{cm}^2} = \frac{\text{g}}{\text{cm sec}}$$

Liquid	Viscosity (cp)
Castor oil	1000
Chloroform	0.563
Ethyl alcohol	1.19
Glycerin, 93%	400
Olive oil	100
Water	1.0019

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- Fluidity (φ)
  - Is defined as the reciprocal of viscosity

$$\varphi = \frac{1}{\eta}$$

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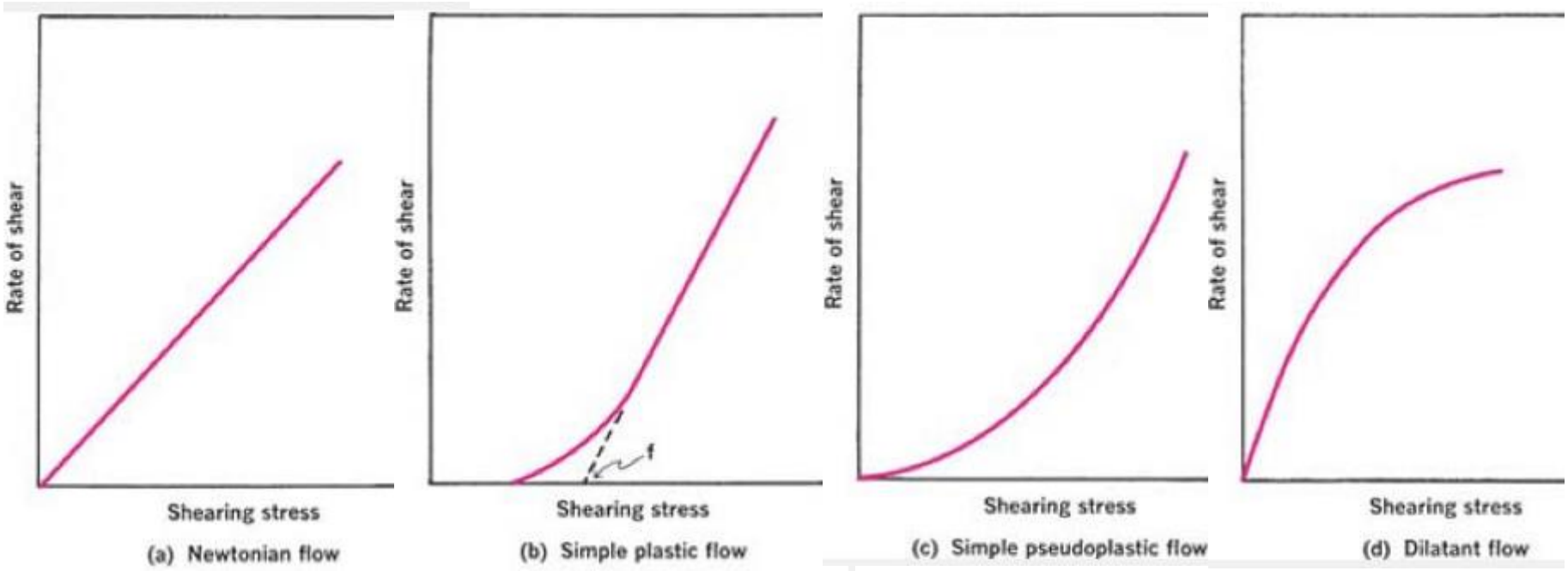
- Rheogram
  - Plot of shearing stress (F) versus rate of shear (G).



- Rheograms are also known as consistency curves or flow curves.
- The rheologic properties of a given material are most completely described by its unique rheogram.
- Rheogram of Newtonian systems:
  - The simplest form
  - Follow the equation for a straight line passing through the origin.

$$G = f \times F$$

  - The slope, f, is known as fluidity (??)

- Rheogram of non-Newtonian systems:
  - Plastic systems ~ the curve is linear only at values of F, beyond its yield value.
  - Pseudoplastic and Dilatant systems ~ the curve is nonlinear throughout the entire range of F values tested.
    - Shear thinning; slope increases with F.
    - Shear thickening; slope decreases with F.
  - Thixotropic systems ~ the curve shows a hysteresis loop

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- Kinematic Viscosity
  - Is the absolute viscosity (η) divided by the density of the liquid at a specific temperature:

$$Kinetic\ Visccosity = \frac{\eta}{\rho}$$

  - The units of kinematic viscosity are the stoke (s) and the centistoke (cs)

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- Temperature and Viscosity
  - Viscosity of a gas increases with temperature(?),
  - Viscosity of a liquid decreases as temperature is raised(?),
  - The fluidity of a liquid (the reciprocal of viscosity) increases with temperature (?),
  - Temperature dependence of viscosity is expressed by an equation:

$$\eta = Ae^{E_V RT}$$

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Non-Newtonian Systems

- The majority of fluid pharmaceutical products are not simple liquids and do not follow Newton's law of flow,
- Non-Newtonian behavior is exhibited by: colloidal solutions, emulsions, liquid suspensions, and ointments.
- Three classes of non-Newtonian flow: Plastic, Pseudoplastic, and Dilatant.

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Plastic Flow

- Bingham bodies?
- Plastic flow curves do not pass through the origin,
  - But, rather intersect the shearing stress axis at a particular point referred to as the yield value (f).
  - A Bingham body does not begin to flow until a shearing stress corresponding to the yield value is exceeded.
  - At stresses below the yield value, the substance acts as an elastic material.

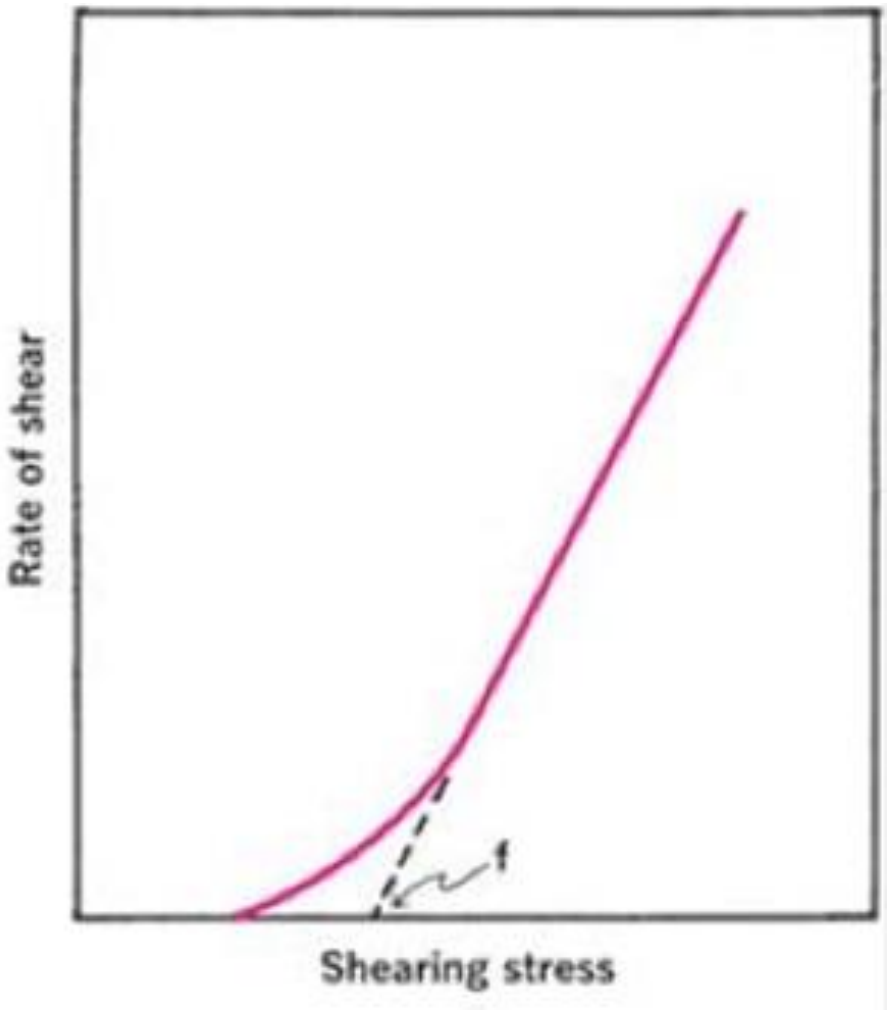

Fig. Rheogram of material showing simple plastic flow.

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- Based on the yield value, materials can be classified (rheologically) as:
  - **Solids** ~ those substances that exhibit a yield value,
  - **Liquids** ~ substances that begin to flow at the smallest shearing stress and show no yield value.
- The equation describing plastic flow:

$$U = \frac{F - f}{G}$$

Where, U is plastic viscosity, and f is the yield value, or intercept

- The slope of the rheogram (inverse of U) is termed the mobility,

- Plastic flow is a characteristics of flocculated suspensions.
  - A continuous structure is set up throughout the system.
  - A yield value exists because of the contacts between adjacent particles which must be broken down before flow can occur.
  - The yield value is an indication of force of flocculation,
  - The more flocculated the suspension, the higher will be the yield value.

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Pseudoplastic Flow

- Many pharmaceutical products exhibit pseudoplastic flow.
  - Pseudoplastic flow is typically exhibited by polymers in solution.
- Curve for a pseudoplastic material begins at the origin, therefore, there is no yield value.
  - And, because the curve is not linear, the viscosity of the system cannot be expressed by any single value.

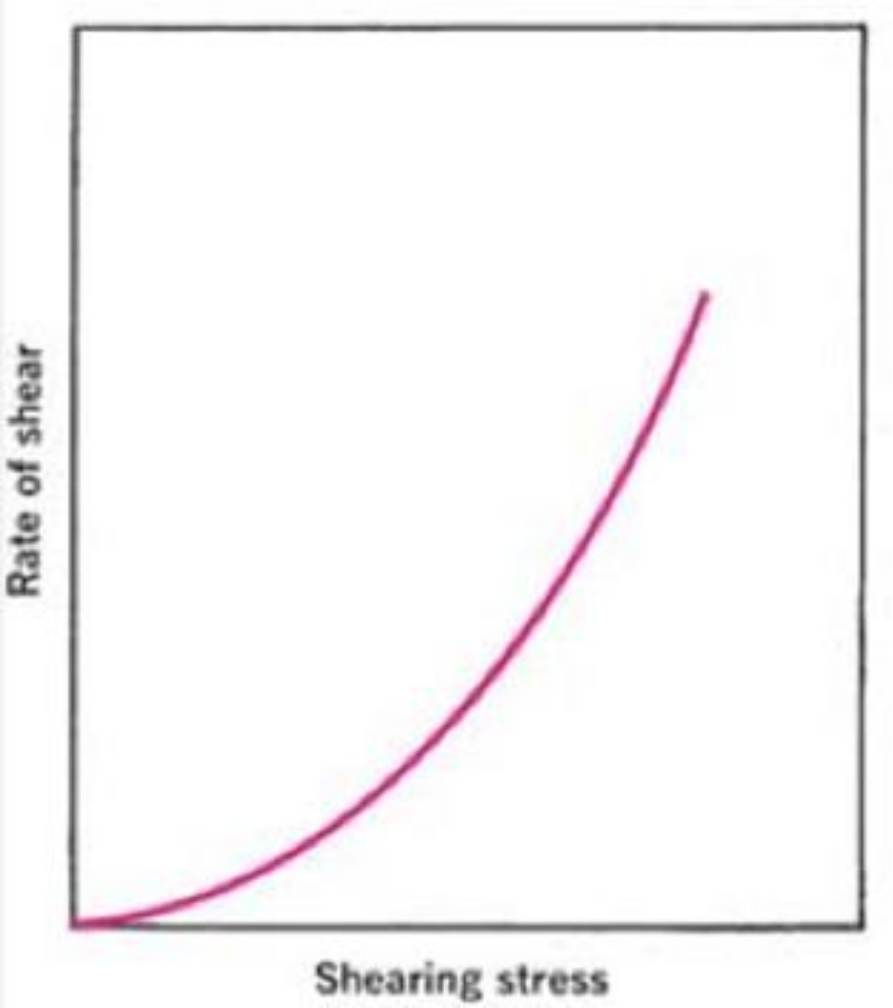

Fig. Rheogram of material showing simple pseudoplastic flow.

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- Objective description of pseudoplastic systems are more difficult than with either Newtonian or plastic systems.
  - Martin and his colleagues tried to use an exponential formula to mathematically describe pseudoplastic system:

$$F^N = \eta' G$$

  - The exponent N rises as flow becomes increasingly non-Newtonian.
  - When N = 1 (?)

- The above equation can be rearranged and written in its logarithmic form,

$$\log G = N \log F - \log \eta'$$

- Many pseudoplastic systems fit this equation when logG is plotted as a function of logF.

- The viscosity of a pseudoplastic substance decreases with increasing rate of shear (?).

  - Shear-thinning systems!!

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Dilatant Flow

- Some materials exhibit an increase in resistance to flow with increasing rates of shear.
  - E.g. some suspensions with a high percentage (about 50% or greater) of dispersed solids
  - Such systems actually increase in volume when sheared and are hence termed dilatant.
    - Shear-thickening systems!!
    - When stress is removed, a dilatant system returns to its original state of fluidity.

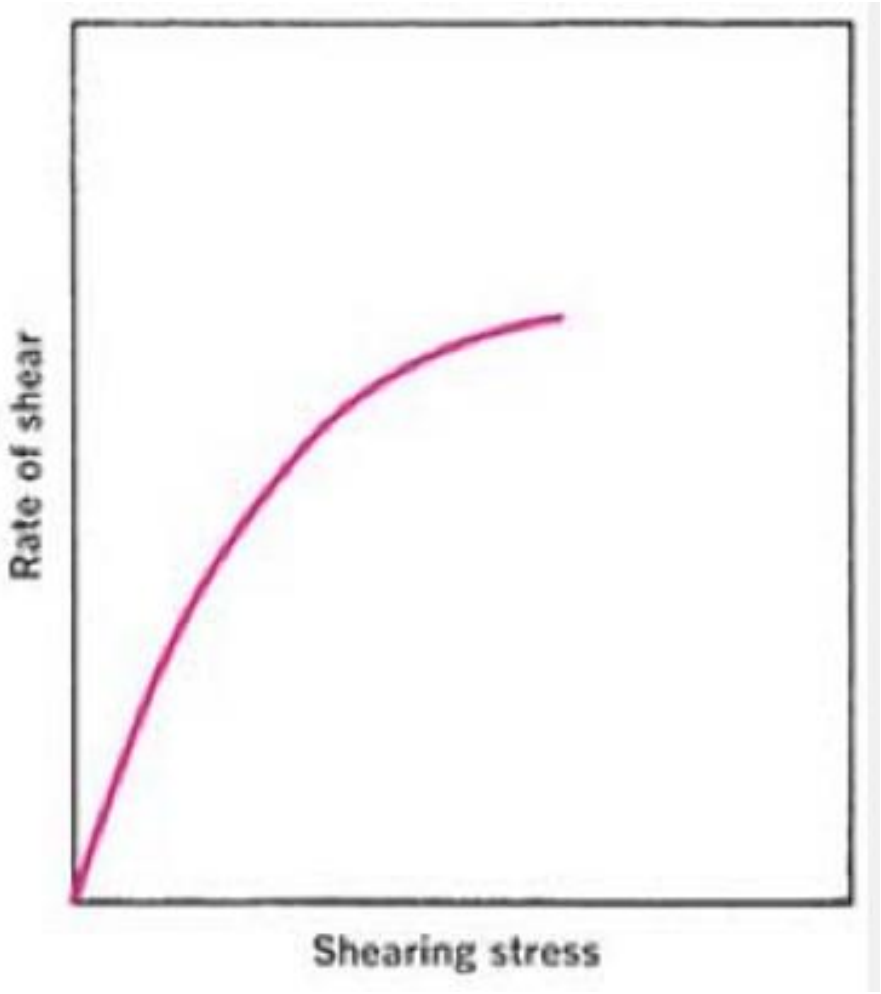

Fig. Rheogram of material showing Dilatant flow.

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Thixotropy

- With increased rate of shear several types of flow behaviors are observed.
  - Newtonian systems ~ down-curve would be identical (superimposable) with the up-curve when shear is reduced (removed).
  - Non-Newtonian systems ~ down-curve may be displaced relative to the up-curve.

- For shear-thinning systems (pseudoplastic), the downcurve is displaced to the left of the upcurve.
  - i.e. the material has a lower consistency at any one rate of shear on the downcurve than it had on the upcurve.
  - This may be due to a breakdown of structure (and hence shear thinning) that does not reform immediately when stress is removed.
  - This phenomenon is known as thixotropy.
  - Thixotropy "an isothermal and comparatively slow recovery, on standing of a material, of a consistency lost through shearing."

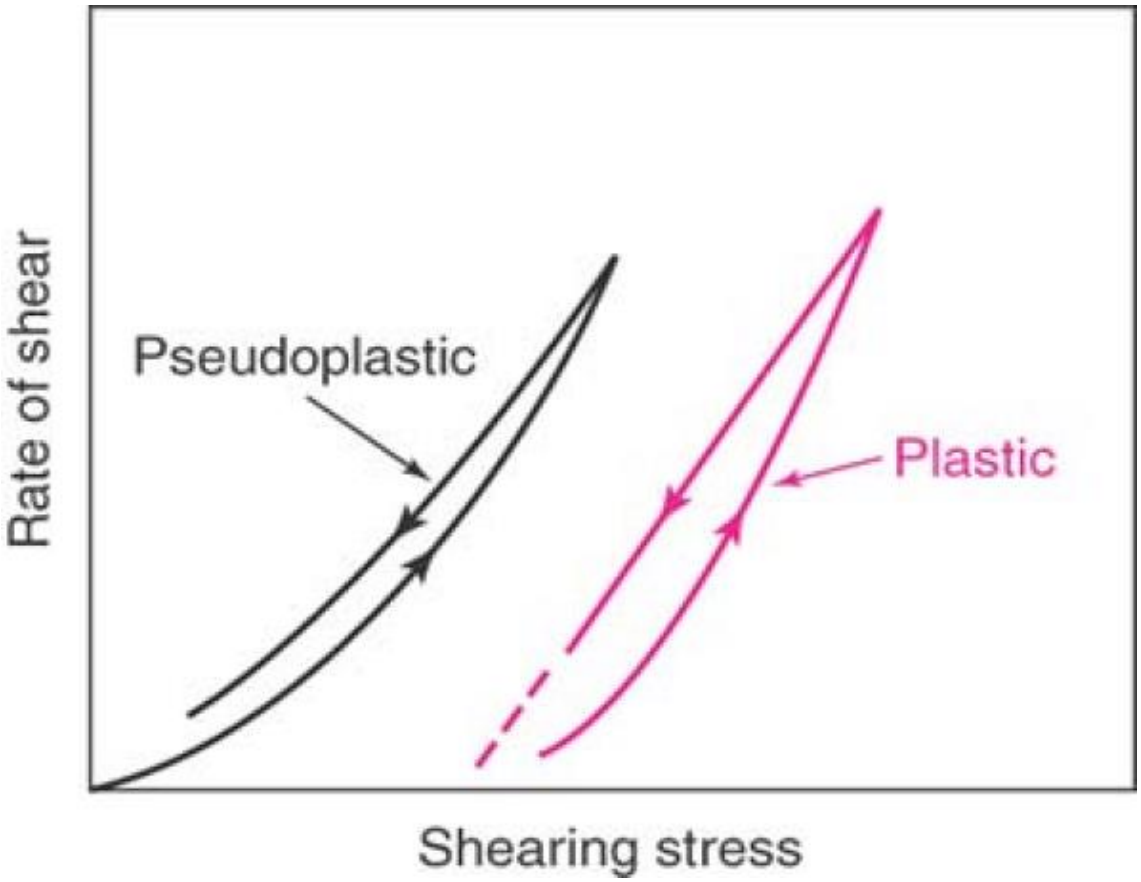

Fig. Thixotropy in plastic and pseudoplastic flow systems.

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Measurement of Thixotropy

- The best characteristic of a thixotropic system is the hysteresis loop.
  - The area of hysteresis has been proposed as a measure of thixotropic breakdown,
  - It can be obtained readily by means of a planimeter or other suitable technique

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- For plastic materials:
  - Two approaches are frequently used to estimate degree of thixotropy
    1. To determine structural breakdown with time at a constant rate of shear
    2. To determine the structural breakdown due to increasing shear rate

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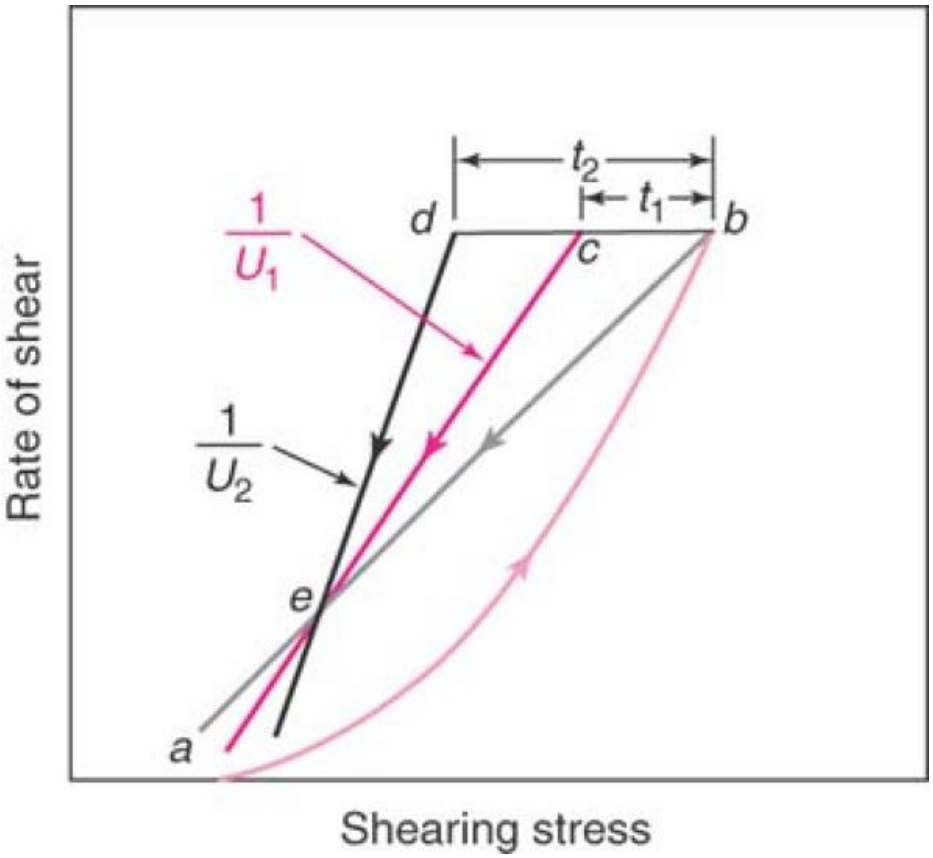
1. Determining structural breakdown with time at a constant rate of shear



- Suppose, in above Figure, the shear rate of a thixotropic material is increased in a constant manner from point ‘a’ to point ‘b’ and is then decreased at the same rate back to ‘e’
- This would result in the so-called hysteresis loop ‘abe’
- If, however, the sample was taken to point b and the shear rate held constant for a certain period of time (t1), and is then decreased at the same rate back to ‘e’
  - It would result in the hysteresis loop ‘abce’
- If the sample had been held at the same rate of shear for t2, the loop ‘abcde’ would have been observed

- A thixotropic coefficient, B, the rate of breakdown with time at constant shear rate, is calculated as follows:

$$B = \frac{U_1 - U_2}{\ln \frac{t_2}{t_1}}$$

- where U_1 and U_2 are the plastic viscosities of the two downcurves.

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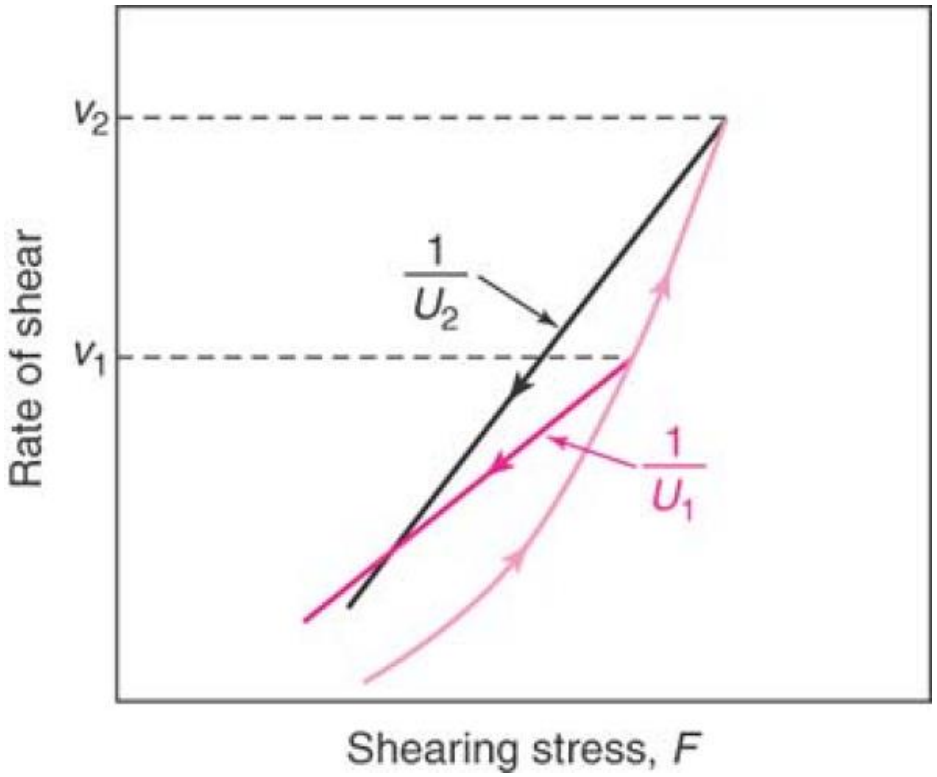
2. Determining structural breakdown with the structural breakdown due to increasing shear rate



- Two hysteresis loops are obtained having different maximum rates of shear, v1 and v2.

- In this case, a thixotropic coefficient, M, the loss in shearing stress per unit increase in shear rate, is obtained by:

$$M = \frac{U_1 - U_2}{\ln \frac{v_2}{v_1}}$$

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Negative Thixotropy

- Represents an increase rather than a decrease in consistency on the downcurve,
- i.e. increase in thickness or resistance to flow with increased time of shear.
- Should not be confused with dilatancy or rheopexy (?)

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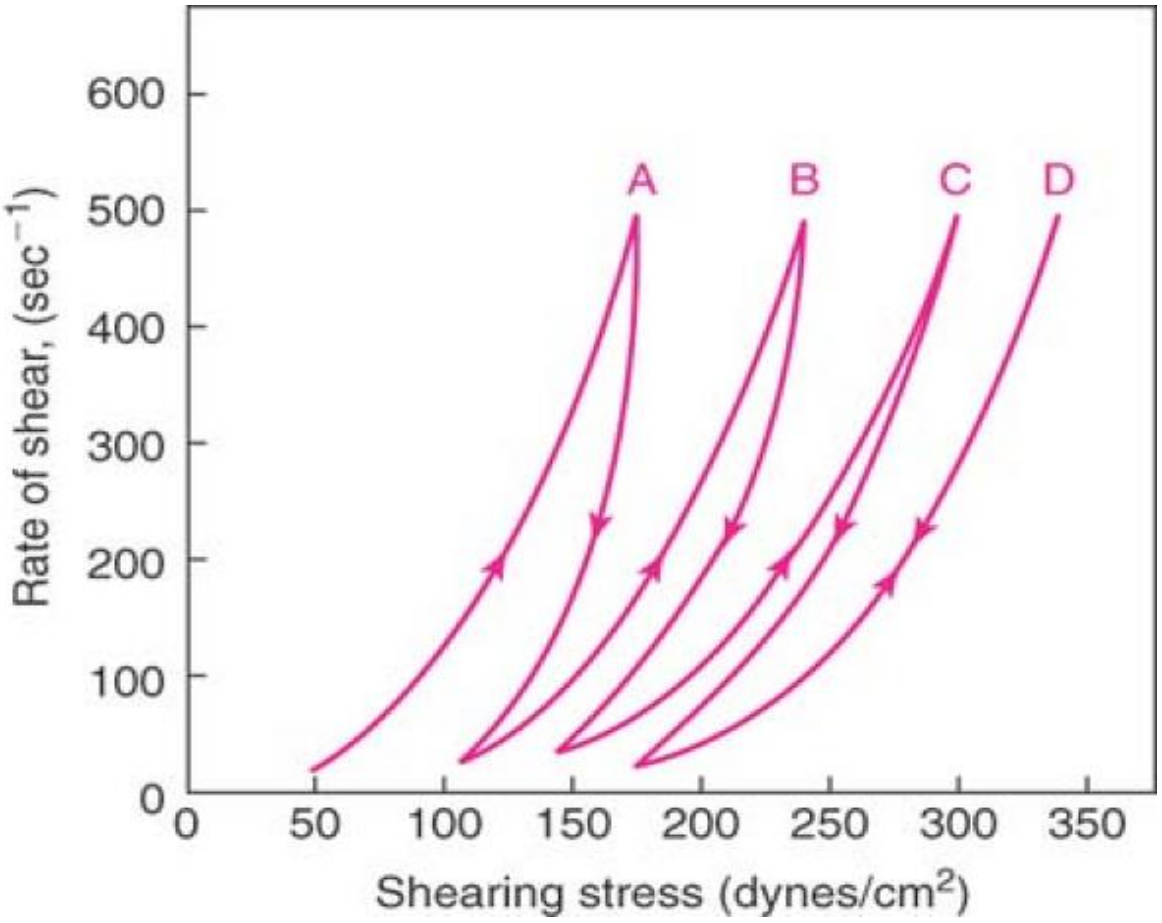

Fig. Rheogram of magnesia magma showing antithixotropic behavior.

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Thixotropy in Formulation

- Desirable property in liquid pharmaceutical systems (?)
  - A high consistency in the container, yet pour or spread easily,
  - E.g. a well-formulated thixotropic suspension (?).
  - A similar pattern of behavior is desirable with emulsions, lotions, creams, ointments, and parenteral suspensions.
  - There is a relationship between degree of thixotropy and rate of sedimentation in disperse systems.

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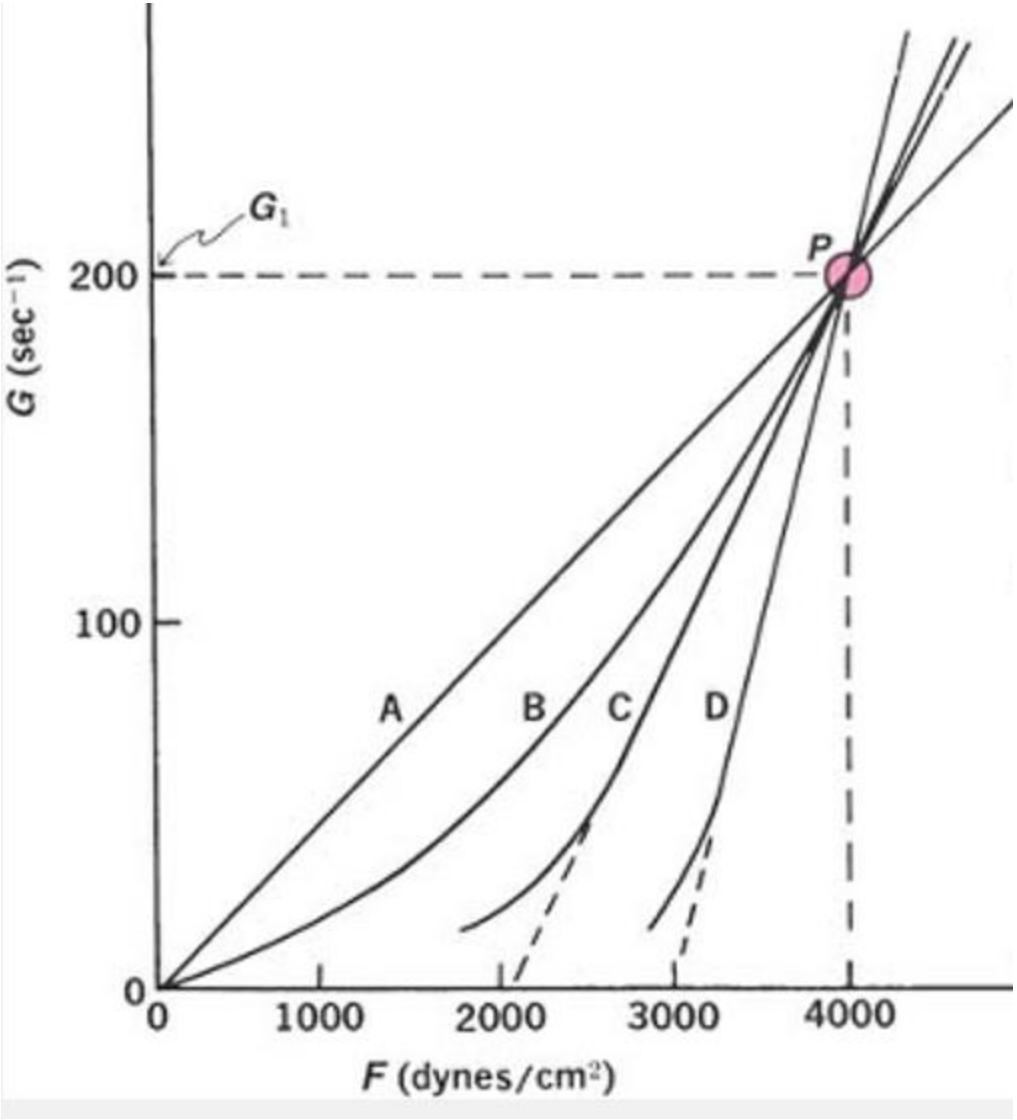
Determination of Rheologic Properties

- Determination and evaluation of rheologic properties is dependent on the instrumental method used.
  - For a Newtonian system ~ instruments that operate at a single shear rate can be used.
  - For non-Newtonian system ~ the instrument can operate at a variety of shear rates.


G_1
P
200
100
0
G (sec⁻¹)
A
B
C
D
0
1000
2000
3000
4000
F (dynes/cm²)

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- All viscometers can be used to determine viscosity of Newtonian systems,
- However, only those with variable–shear-rate controls can be used for non-Newtonian materials.
- Commonly used types of viscometers:
  - Capillary viscometer
  - Falling-sphere viscometer

  } Single–shear-rate instruments suitable for use only with Newtonian materials

  - Cup-and-bob viscometer
  - Cone-and-plate viscometer

  } Multipoint, rotational instruments can be used with both Newtonian and non-Newtonian systems

Capillary Viscometer

- Known as an Ostwald viscometer
  - Determines viscosity by measuring the time required for the liquid to pass between two marks as it flows by gravity through a vertical capillary tube.
  - The time of flow of the liquid under test is compared with the time required for a liquid of known viscosity (usually water) to pass between the two marks.

$$\frac{\eta_t}{\eta_s} = \frac{\rho_t t_t}{\rho_s t_s}$$

- Where, t – for test liquid, and s – for standard liquid
- The value $\frac{\eta_t}{\eta_s} = \eta_{rel}$ is known as the relative viscosity of the liquid under test.
- The above equation is based on "Poiseuille's law" for a liquid flowing through a capillary tube:

$$\eta = \frac{\pi r^4 t \Delta P}{8 \times h \times V}$$

Falling-Sphere Viscometer

- Hoeppler viscometer
  - A ball rolls down in vertical glass tube containing the test liquid at a known constant temperature.
  - The rate at which a ball falls is an inverse function of the viscosity of the sample.
  - The time for the ball to fall between two marks is accurately measured and viscosity of a Newtonian liquid is then calculated:

$$\eta = t\left(S_b - S_f\right) \times B$$

- t – time for the ball to fall
- S_b and S_f are the specific gravities
- B is a constant for a ball

Cup-and-Bob Viscometer

- The sample is sheared in the space between the outer wall of a bob and the inner wall of a cup into which the bob fits.
- Two types
  - Couette type ~ the cup is rotated (MacMichael viscometer)
  - Searle type ~ uses a stationary cup and a rotating bob (Rotovisco viscometer)
    - Can also be modified to operate as a cone and plate instrument.

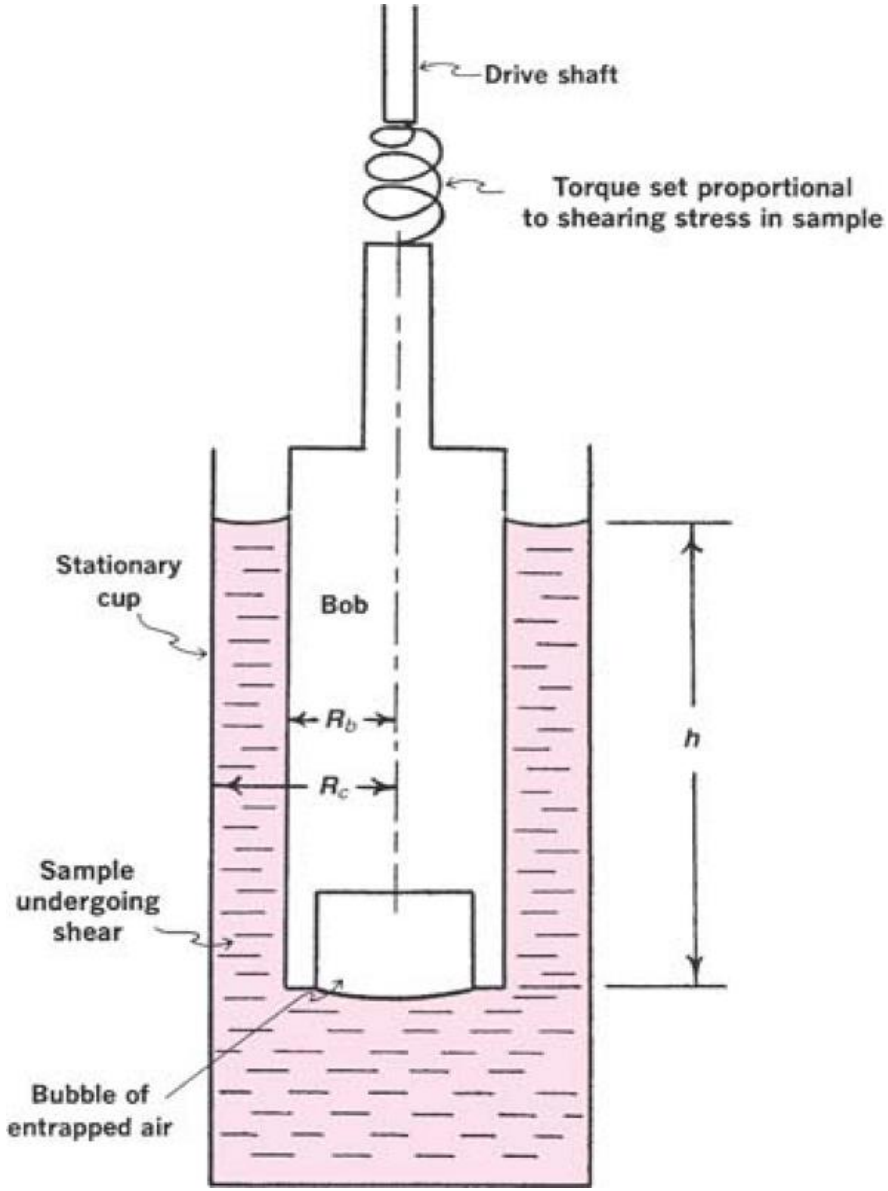

Fig. Principle of rotational cup-and-bob viscometer (Searle type).

- Popular viscometers based on the Searle principle is the
  - Stormer viscometer
  - Brookfield viscometer

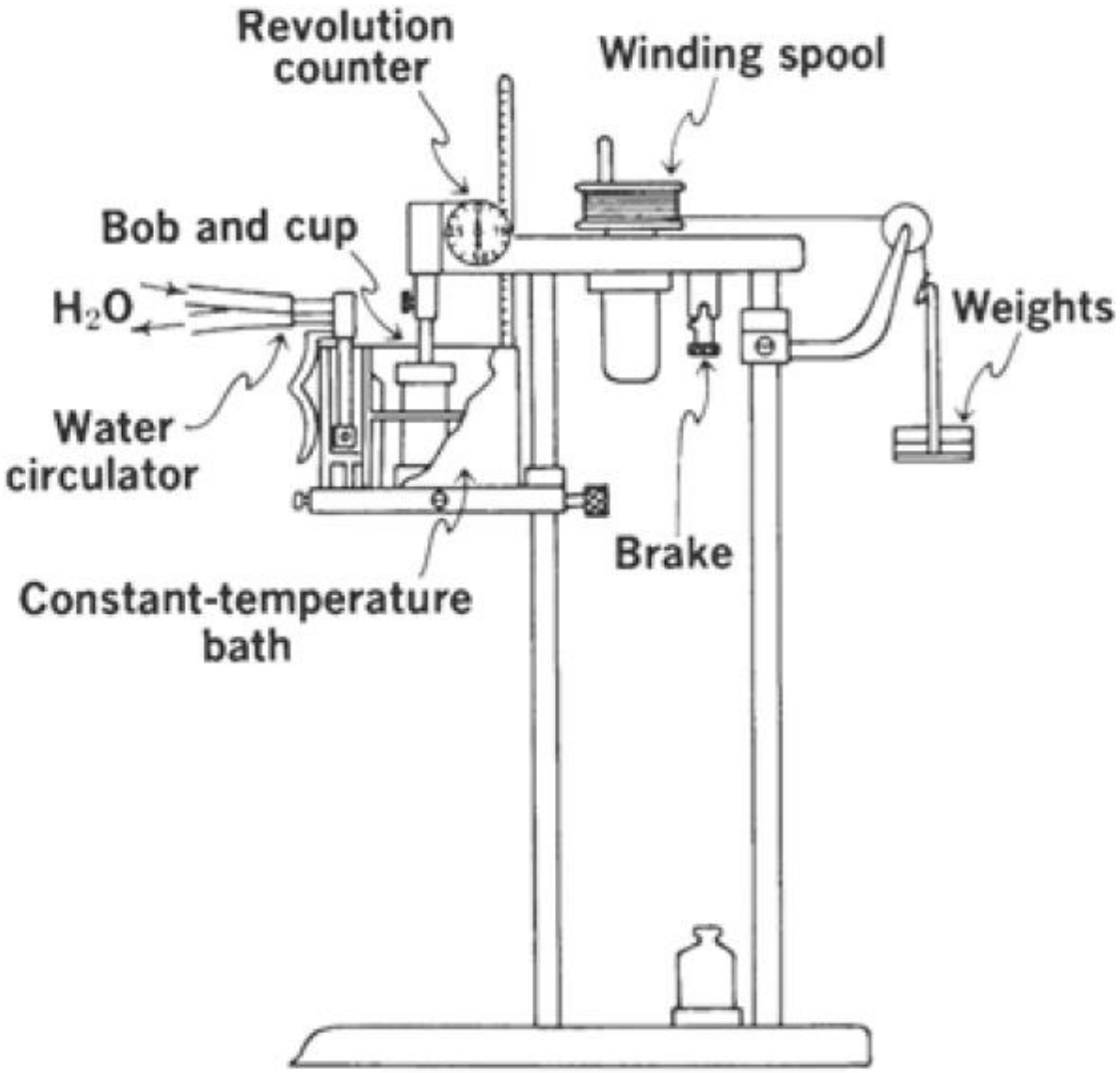

Fig. Stormer viscometer.

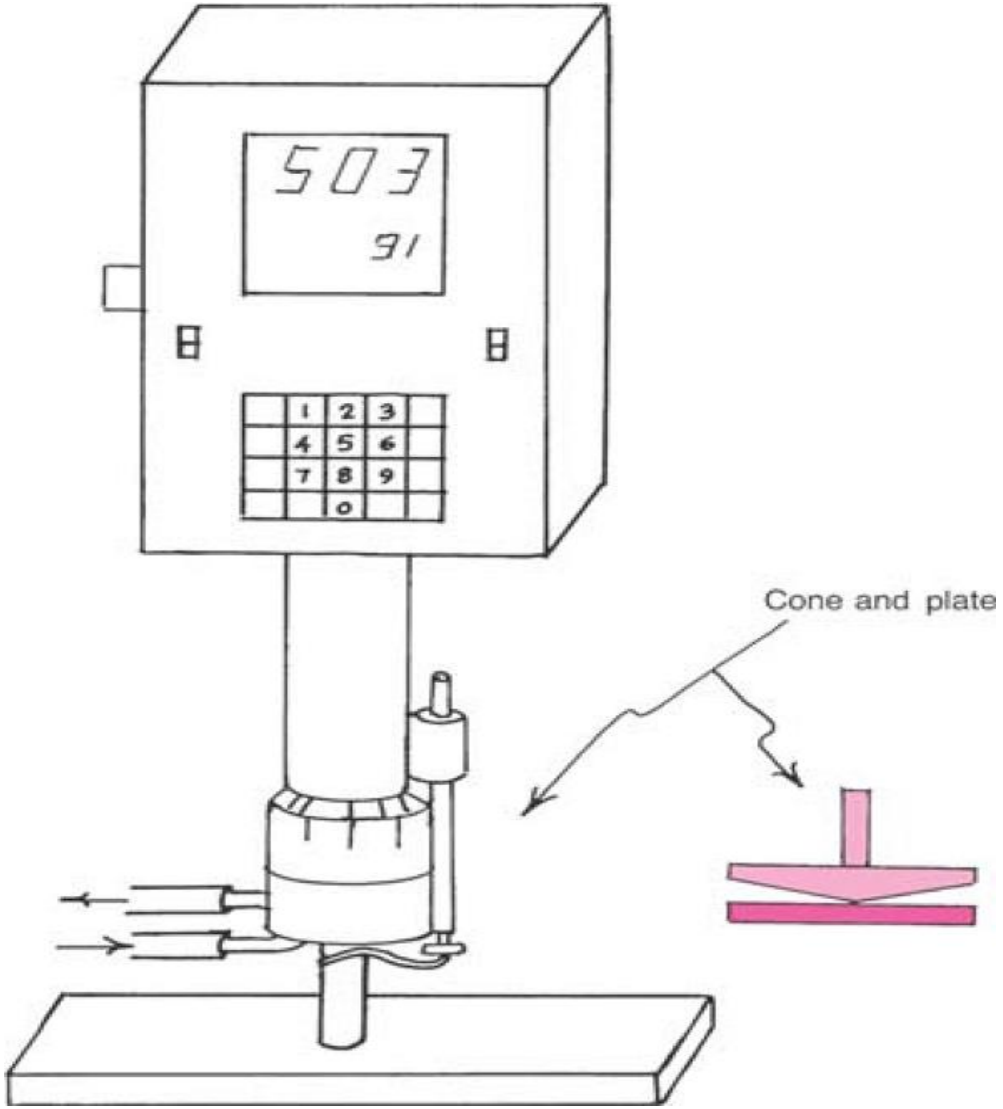

Fig. A digital-type cone-and-plate Brookfield viscometer.

Cone-and-Plate Viscometer

- Ferranti–Shirley viscometer ~ Rotational cone-and-plate viscometer
  - The sample is placed at the center of the plate,
  - Then raised into position under the cone,
  - A variable-speed motor drives the cone,
  - The sample is sheared in the narrow gap between the stationary plate and the rotating cone.

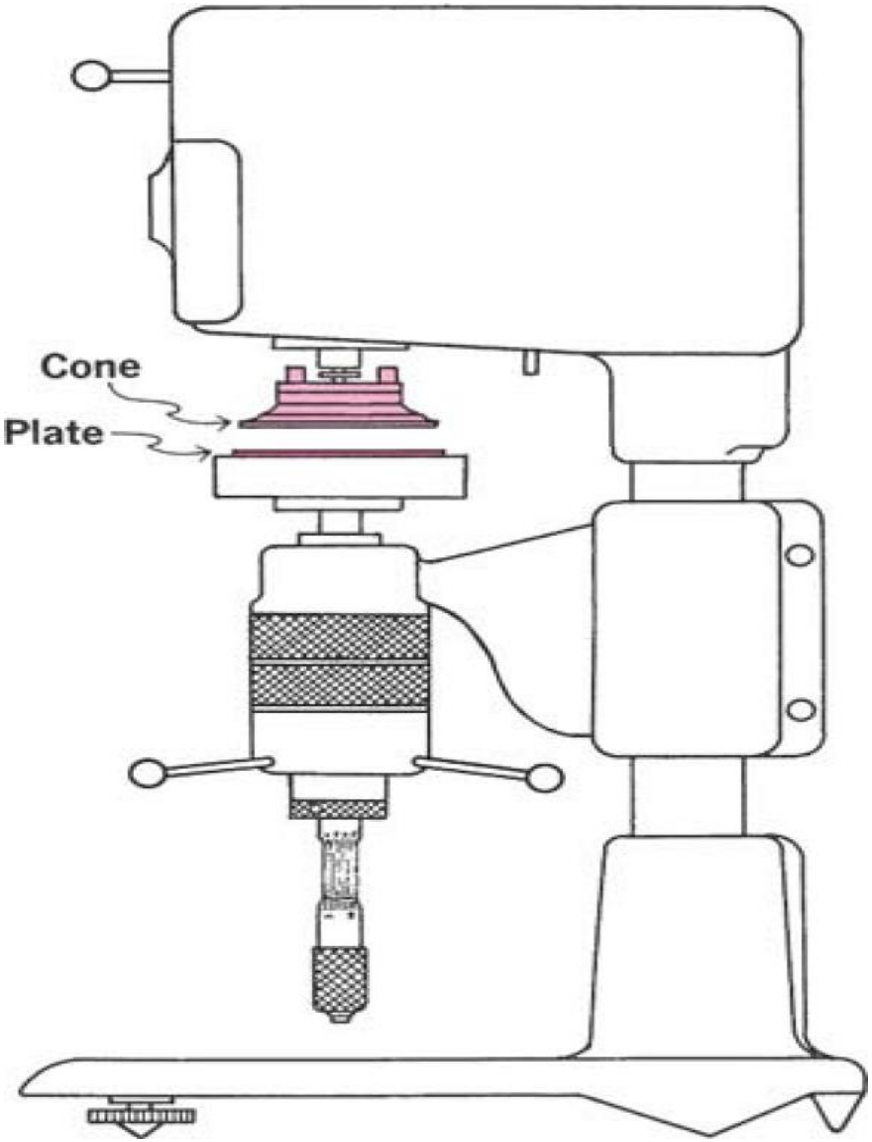

Fig. The measuring unit of the Ferranti–Shirley cone–plate viscometer.

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Viscoelasticity

- The Rheologic characterizations discussed further centered on the fundamentals of continuous or steady shear rheometry of non-Newtonian materials.

- Oscillatory and creep measurements are also of considerable importance for investigating the properties of viscoelastic materials.

  - Many of pharmaceutical semisolids and disperse systems belong to this class.

- Rotational viscometers (with steady shear)
  - Continuous shear does not keep the material being tested in its rheologic “ground state”
  - It resorts to gross deformation and alteration of the material during measurement.
  - Such instruments yield large deformations and may produce false results.

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- Oscillatory and creep methods
  - Allow the examination of rheologic materials under nearly quiescent equilibrium conditions.
  - Analysis of viscoelastic materials is designed instead not to destroy the structure.
  - Viscoelastic measurements are based on the mechanical properties of materials that exhibit both viscous properties of liquids and elastic properties of solids.

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- A semisolid is considered to demonstrate both solid and liquid characteristics.
  - The flow of a Newtonian fluid is expressed by:

$$\eta = \frac{F}{G}$$

  - A solid material is not characterized by flow but rather by elasticity, and by the equation for a spring (Hooke's law):

$$E = \frac{F}{\gamma}$$

where E is the elastic modulus (dyne/cm2), F is the stress (dyne/cm2), and γ is the strain (dimensionless).

- Using a mechanical model,
  - A viscous fluid can be represented as movement of a piston in a cylinder (or dashpot) filled with a liquid,
  - An elastic solid is modeled by the movement of a Hooke spring.
  - The behavior of a semisolid as a viscoelastic body can therefore be described by the combination of the dashpot and spring,
  - Combined in series ~ called a Maxwell element
  - Combined in a parallel arrangement ~ Voigt element

- - -

(a) Dashpot

(b) Spring

(c) Dashpot and spring in series (Maxwell unit)

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Pharmaceutical Applications of Rheologic principles

- Fluids
  - Mixing
  - Particle-size reduction of disperse systems with shear
  - Passage through orifices, including pouring, packaging in bottles, and passage through hypodermic needles
  - Fluid transfer, including pumping and flow through pipes
  - Physical stability of disperse systems

- Quasi-solids (semisolids)
  - Spreading and adherence on the skin
  - Removal from jars or extrusion from tubes
  - Capacity of solids to mix with miscible liquids
  - Release of the drug from the base

...

- Solids
  - Flow of powders from hoppers and into die cavities in tabletting or into capsules during encapsulation
  - Packagability of powdered or granular solids
- Processing
  - Production capacity of the equipment
  - Processing efficiency